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# CHEMISM OF ACUTE WEIGHT LOSSES
# RELATION BETWEEN WATER AND SALTS IN THE ORGANISM

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ABSTRACT

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The material, available from the literature, on weight losses as a function of environmental or test conditions is discussed, especially with respect to weight losses in infants. To study the physiological and chemical processes in weight losses, experiments were performed to determine the amount of water in weight losses and to investigate the chemical composition of the material lost. For this purpose, diarrhea was generated in test animals (dogs) by administering large doses of magnesium sulfate into the stomach. The resulting losses of water and weight were so large that the animals finally died. The pathological conditions observed were somewhat similar to those which occur in severe nutritional disturbances of infants.

Author

The losses of body substance (including water) were determined from the differences between the test animals and control animals, both of the same brood. A determination was made of the control and the test animals; absolute and relative contents of the fat and fat-free residue: total N, dry substance; ashes (from the dry substance); from the latter: Cl, P, Ca, Mg, alkali, Si and S.

The weight losses, the organs' weights and their losses, the contribution of the individual organs to the total weight loss and the percentage of the organs' constituents (water, fat, dry substance, N, and ashes) and the percentage reduction of the components are listed in the form of tables. Other tables show the components of the ashes and their decrease in the experiment, referring especially to the minerals. 65 - 70% of the total weight loss are contributed by water, 25 - 30% by fat, 4 - 5% by the dry substance.

The last section of the article deals in detail with the reduction of K and Na and other minerals. The result is that the percentage losses of Cl and K are largest, followed by those of Na and Si. The losses of those substances in skin and subcutaneous tissue (which are called "soft parts" throughout this paper), are related to those of water, but the mineral losses occur at a slower rate than those of water. The mineral losses of the organs are such that the percentage composition of the internal organs remains practically unchanged.

The author classifies the water losses, according to their extent and consequences, into three types: concentration water losses - which can be restored rapidly and easily; reduction water losses - in which an essential part of the body's water is lost, yet can be restored within some length of time; destructive water losses - which imply danger to the life of the individual due to their large extent.

Fluctuations, and continuous variations of the body's weight, to a degree observed only in exceptional cases in adults - and then mostly in severe disturbances of water excretion - are quite common with young children. In the course of grave, acute nutritional disturbances, infants may lose up to a third of their weight within a short time, even without diarrhea. On the other hand, during convalescence after such catastrophic disturbances one can occasionally see the body weight rise just as rapidly without visible edema resulting. With some forms of nutrition, especially sudden changes in the food composition, temporary weight fluctuations are common; they may be of an extent which greatly exceeds the normal weight increase of a healthy child or the weight losses due to hunger. Freund (1) discussed this in detail and showed that such weight variations must originate predominantly from variations in the water content of the body. This follows most likely from the fact that 100 g of the body substance of a new-born infant contain 71.8 g /432 /431*

(1) W. Freund. Water and Salts in their Relation to Weight Fluctuations of Infants. Jahrb. f. Kinderheilkunde, Vol. 59, p. 421, 1904.

* Note: Numbers in the margin indicate pagination in the original foreign text.

of water, but only 15.9 g of solids and 12.3 g of fat. Proportional variations of the water content are therefore naturally of a larger order of magnitude than those of the rest of the constituents. From the highest positive or negative balances resulting from metabolism experiments, it is not possible to calculate values for protein, fat or even ashes that can correlate with the weight values with which we are concerned. The role of water exchange in large weight fluctuations over short periods has not been disputed by anybody (e.g., see Czerny and Steinitz [1], L. F. Meyer[2]).

The situation becomes more complicated if one wishes to determine whether other components and - if so - which ones, necessarily accompany the water transport. As a matter of fact, numerous investigations in recent years could explain - to a considerable extent - the chemical mechanism of *pathological* water accumulations in the body. This mechanism is governed by the sodium chloride metabolism. In certain disease conditions, when sodium chloride is administered, up to several kilograms of water can be deposited in the form of an edema or as an effusion in the body; salt deprivation reduces the edemas within a short time while simultaneously flushing out the salt. These effects, which may also occur at a very early age, call for a comparison with those described above for infants. However,

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(1) Von Noordens. Handbuch der Pathologie des Stoffwechsels (Handbook of Metabolic Pathology), Vol. 2, p. 429, 1906.

(2) L. F. Meyer. Nutritional Disturbances and Salt Metabolism of Infants (Ernäbrungsstörungen und Salzstoffwechsel beim Säugling). Ergebnisse d. inneren Medizin u. Kinderheilkunde, Vol. 1, p. 317, 1908.

one should not neglect a basic difference in the two processes: in the one case we are dealing with the addition and removal of the physiological constitutional water of the organism, while in the other case we are concerned only with the water which is superimposed on the body's water and deposited in pathological form. The latter reveals its particular nature by its instability (lability), even when it is not yet palpable as edema, but recognizable only by the additional weight. With healthy persons who have a sufficient chloride level, administration of common salt does not affect their weight or - if the common salt is given in large doses - it even has a dehydrating effect. Administration of common salt to infants with nutritional disturbances during recovery frequently leads to an even sharper increase in the weight curve, with simultaneous appearance of edemas, whereas before a diet deficient in /433
sodium chloride resulted in water deposition without edema.

Thus, the water exchange governed by NaCl is - at first sight - only a special case of primarily pathological interest. Although most people implicitly assume that the physiological water content and its disturbances depend only on the amount of common salt; the question of how the main quantity of normal body water is bound and excreted, still remains unanswered. Precise and sufficient data to answer this question is still not available. It is generally assumed that the organism excretes salts only in aqueous solution, and never excretes water in chemically pure form. This also coincides best with daily observations. And yet, however, the fact remains that the body is able to dispose of large amounts of its water as water vapor through the lungs.

Freund[1] found that diarrhea stools are richer in chlorine than normal stools, and he believes that it is not water, but a sodium-rich salt solution that transudes into the intestines. He also discovered that chlorine is retained when the quantity of water in the organism increases; he is of the opinion that salt retention is the indicator of water deposition, even when the weight remains unchanged. However, he was occasionally able to establish the fact that chlorine was also retained during weight losses. In one test, a retention of alkali was observed during weight increase, in which the alkali amounted to approximately the quantity of chlorine retained. But even these meager data can be used only to a limited extent, because the test setup, in which the metabolism's dependence on a sudden change of food was investigated in all cases, implies conditions for the mineral metabolism which are so complicated that the relation between water and salts are by no means unambiguously clear.

Meyer [2] expresses himself in a more cautious and less specific way than Freund. He does not restrict himself to the non-pathological cases, and suggests that besides the alkali, chlorine may be closely related to the water balance in the body. The fact that Meyer [3]

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(1) W. Freund. Chlorine and Nitrogen in the Infant Organism. (Chlor und Stickstoff im Säuglingsorganismus.) Jahrb. f. Kinderheilkunde, Vol. 48, p. 137, 1898.

(2) Loc. cit, p. 326.

(3) Meyer, L.F. Importance of Mineral Salts in Nutritional Disturbances of Infants (Die Bedeutung der Mineralsalze bei den Ernährungsstörungen des Säuglings). Proceedings of the Society for Child Medicine (Verhandlungen d. Gesellschaft f. Kinderheilkunde). Salzburg, p. 14, 1909.

recently - based on experiments in which various salts were added to food , came to the conclusion that water accumulation is dominated by Na ions - means that these experiments are connected with pathologi- /434 cal water buildups which are of a transient nature. - The salt losses of infants with certain nutritional disturbances are more closely related to fat metabolism than to water exchange. The processes of mineral metabolism in the weight losses of "poisoning" have barely been investigated. In such a case, Meyer found a slight common salt decrease of 0.0806 g after three days.

To date, chemical investigations in clinics could not elucidate the relation between the physiological water and the salts of the body. However, this problem is of the greatest importance in order to obtain an insight into the nature of nutritional disturbances, in which huge water losses predominate, and to interpret the success and failure of nutritional therapy.

Before a scientific analysis of the complicated interrelated processes of clinical weight losses could provide results, it appeared necessary to study the pathological physiology of acute water losses under the more easily controllable and more clearly arrangeable conditions of animal experiments. From the results obtained, one might hope to proceed to a more correct formulation of the problems.

At first, we wanted to determine the relative amount of body weight that can be lost through experimentally-generated diarrhea, and how large the short-term substance losses have to be in order to be fatal.

The question then arose concerning the parts of the body involved in the total weight loss and the relative contribution of each part. In addition, the chemical components of a given weight loss had to be determined, especially the percentage of water. Finally, we were especially interested in the question of to what extent, and in what fashion is the chemical composition of the organism changed after water losses exceeding the normal water percentage in the composition of the body structure under consideration, and what chemical components are necessarily related to the release and the incorporation of physiological body water.

Within the scope of these questions, a number of animal experiments have been performed on the effect of thirst on weight and water exchange of the organism, or of individual organs. The dehydrating effect which thirst has on the organism is relatively small, especially if it is accompanied by total food deprivation. In this case, the constitutional water which is set free during the reduction of the /435
body substance approximately makes up for the unavoidable water expenditures; the percentage of water in the body may even be increased. The situation becomes different if food containing little water is eaten or administered; then the metabolic end products extract from the body's supply the water which is necessary for their excretion, whereas other body components remain conserved. Observations show that thirsty animals after a short time of water deprivation instinctively refuse food deficient in water, even when they are hungry.

Schuchardt [1] reports on water deprivation experiments with pigeons which were fed with barley dried in the air; they died usually after approximately 11 days, and lost on an average 43.9% of their body weight. Animals exposed to hunger and thirst lived only for half that time and lost 34% of their weight. The breast muscles were diminished most among all the organs; in the thirst experiments they were reduced by 37%; in the experiments with total deprivation, by 34%.

After 12 - 13 days of thirst, Sheffer's pigeons [2] died when they had been fed with wheat; they had lost an average of 45.8% of their body weight. A thirsty dog [3], which received biscuits until he refused any food, lost 20% of its weight during a 28-day experiment. Comparison with another animal of the same brood, which was killed at the beginning of the experiment, showed that the skin with 25% loss and the muscles with 54% loss were the most important contributors to the total loss. The water content of almost all the organs was reduced; the greatest losses involved the skin and muscles. The entire animal contained only 4% less water than a comparison animal.

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(1) B. Schuchardt. Quaedam de effectu, quem privatio singularum partitum etc. (On the Effect which Deprivation of some Parts, etc.). Dissertation, Marburg, 1847.

(2) Scheffer. De animalium, aqua iis adempta, nutritione (On the Nutrition of Animals Deprived of Water). Dissertation, Marburg, 1852.

(3) See also Falck and Scheffer. Investigations on the Water Content of Organs of Dogs Deprived and Not Deprived of Water (Untersuchungen über den Wassergehalt der Organe durstender und nicht durstender Hunde). Arch. f. physiolog. Heilkunde, Vol. 13, p. 508, 1854.

Nothwang [1] increased the effect of water deprivation by forcing the test animals (pigeons) to eat dry peas rich in protein; he could thus reduce to a certain extent the undesired complications which result from the simultaneous voluntary abstaining from food. The water loss obtained amounted to 22.2% during tests of 6 - 7 days. Nothwang /436 determined the dry substance in muscle samples and in the entire animals and found that the animals died once the dry substance of the entire body (which amounted to approximately 26.9% in the normal animal) had increased to 33.47% while the water content had diminished to 66.57%; the dry substance of the muscles increased simultaneously from 23.04 to 29.37%. The percentage of ashes in the fat-free muscles was hardly reduced, however, it was clearly reduced in the case of animals deprived of food. Nothwang proved that in animals deprived of water, decomposition products are retained and thus solid substance is accumulated in the organism.

The experiments of Straub [2], performed with dogs deprived of water and fed with dry meat powder, showed that the muscle substance had lost approximately 20% of its water in a weight loss of 8.4%. According to him, water deprivation leads to an increase of the protein decomposition which continues until the normal water content of the body has been restored.

(1) J. Nothwang. The Consequences of Water Deprivation (Die Folgen der Wasserentziehung). Dissertation, Marburg, 1891.

(2) W. Straub. On the Effect of Water Deprivation on Metabolism and Circulatory System (Über den Einfluss der Wasserentziehung auf den Stoffwechsel und Kreislauf). Zeitschrift f. Biologie, Vol. 38, p. 537, 1899.

These experiments show conclusively that upon water deprivation, losses of the body's weight occur which vary with the conditions of the experiments; these losses do not occur in the same relative amount in all organic systems and the greater they are and the more rapidly they are taking place, the earlier they arrive at the point when the life of the test animal is endangered. The chemical tissue components do not contribute to the weight loss in a ratio corresponding to their normal percentage; first of all, the water of the body is affected and it is reduced the more rapidly, the larger the weight loss. The result of this water loss is a body that is enriched in dry substance.

The normal water distribution in the organism seems to be the reason for the fact that skin and muscles suffer the main part of the water losses. As Bischof [(1)], Volkmann[(2)], Voit[(3)], Bidder and Schmidt[(4)] established, these organs not only belong to the ones with the relatively greatest content of water, but because of their large masses they store the largest part of the total amount of body water. It is of special interest, although not directly related to the problems with which we are concerned here, that these organs, which are

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(1) Zeitschrift r. rationelle Medizin, Vol. 20, p. 75, 1863.

(2) Transactions of the Royal Saxonian Society of Sciences at Leipzig. Math.-Phys. Division (Verhandlungen d. koeniglich sächsischen Gesellschaft der Wissenschaften zu Leipzig. Math.-phys. Classe). p. 202, 1874-75.

(3) Zeitschrift f. Biologie, Vol. 30, p. 513, 1894.

(4) The Digestive Secretions and the Metabolism (Die Verdauungssäfte und der Stoffwechsel). 1852.

normally the ones richest in water, have the greatest capacity for /437 a temporary storage of excess water, or of water accumulated in pathological form. Engels [1] found that - except for the kidneys - skin and muscles have the greatest capacity. The muscles, which contribute approximately 4/10 of the body's weight, are capable of storing more than 2/3 of the excess water introduced via the blood circulation. Water deprivation under other test conditions has a stronger and more rapid effect than water deprivation alone. If concentrated salt or sugar solutions are introduced into the blood circulation, a remarkable dilution of the blood occurs after only a few minutes. The tissue provides amounts of water which make the foreign substance innocuous, or eliminate it. The strong diuresis, starting afterwards, removes considerable amounts of water from the body (Klikowicz[2], Münzer[3], Brasol[4], Magnus[5]). Interesting experiments by Moritz[6]

(1) W. Engels. The Role of the Tissues as Water Deposits (Die Bedeutung der Gewebe als Wasserdepots). Arch. f. experimentelle Pathologie u. Pharmakol, Vol. 51, p. 346, 1904.

(2) Archiv f. Physiologie, p. 518, 1886.

(3) Archiv. f. experimentelle Pathol. u. Pharmakol., Vol. 41, p. 74, 1908.

(4) Archiv. f. Physiologie, p. 211, 1884.

(5) Archiv. f. experim. Pathol. u. Pharmakol, Vol. 44, p. 68, 1900.

(6) Deutsches Archiv f. klin. Medizin, Vol. 41, p. 395, 1887.

- he injected 25% NaCl solution into the abdomen - produced an increase of the dry substance in muscles and skin after the experiment had been in process for 18 minutes.

The experiments cited above treat, or are concerned with, some aspects of our problem. But even these are not completely satisfactory - in part because the test animals (pigeons) are too remote from human beings for comparison - and partly because the weight losses obtained did not occur rapidly enough, nor did they amount to satisfactory quantities. The various kinds of water deprivation cannot be considered as equivalent with respect to their effects. The last experiments either extended over only a short testing period, and were conducted in such a manner that recovery took place, or death occurred after not more than three hours test duration (Moritz); the latter was not only due to water deprivation. In both cases, the material can contribute only little to the question with which we are concerned.

It appeared necessary for a solution of our problem, to attain /438
a weight loss as huge as possible within a time interval as short as possible, so that the changes would be large enough to exceed the not quite negligible errors of the experiment and - on the other hand - that the unavoidable effect of hunger remained very small compared with that of thirst. Both were achieved by profuse, watery diarrhea, caused by administering large amounts of magnesium sulfate through a tube into the stomach (for details, see below). When weight determinations of the individual organs revealed that the weight losses

originated 60 - 70% from the soft parts (skin, subcutaneous tissue and muscles), the chemical composition of the weight losses in these materials was investigated. It seemed that this procedure could give, in more than one respect, the clearest answer to our questions.

An exact list of the water and the components either would require equipment which we did not have at our disposal, or would involve considerable error; it would also not permit separation of the processes - which are more closely related to the water exchange - from the results of the total metabolic exchange. Partially because of this reason, partially because the interest concentrated especially on the relation between the individual ash components and the water, the chemical investigation of the total body could not be performed. Since, according to the investigations of Volkmann [1], in humans 83.2% of the body's total ashes are supplied by the skeleton, the ash values from bones would have greatly distorted the small figures which had to be expected, and which are of particular interest. This procedure appears the more justified since - according to the water deprivation experiments of the above-mentioned authors - the skeleton contributes only negligible amounts to the weight loss.

The experimental arrangement chosen makes it necessary to calculate the composition of the losses in test-animal body substance from the weight differences with respect to the healthy control animal. In this way, the assumption is made that the animals used for the test have the same percentage compositions at the start of the experiment.

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(1) Loc. cit.

No doubt this assumption makes certain experimental errors likely. According to the investigations of C. Voits [(1)], the chemical compositions of animals of the same weight cannot be assumed to be identical, since especially due to the varying individual fat content, large errors may be obtained not only for fat, but as a computational result of the fat differences, also for water. The differences in the manner of previous nutrition affect to a large extent the constitutional differences. /439

These sources of error can be reduced to a minimum by comparing only animals of one brood. In the first series, we had two extremely similar animals of a brood. They were 6 weeks of age and were said to have been nursed by their mother until the day we purchased them. For the second series, we selected - from a larger brood of our own breeding - young dogs (those animals which were most similar in weight and constitution). As Falk and Scheffer were able to show, under these conditions the differences in the chemical composition of young dogs are so small that they may justifiably be neglected. Until the beginning of the experiment (at an age of three weeks), the animals were nursed only by the mother animal. The figures from our report, make a great similarity appear very likely for these "parallel" animals.

The experiments were made in two series, the first of which involved two, and the second, three animals. The test was preceded by one day of food deprivation to empty the intestinal tract. The relatively large losses (also of mineral substances) on the first day of

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(1) Zeitschr. f. Biologie, Vol. 2, p. 307, 1866.

food deprivation are therefore eliminated from our experiments.

At the end of the day before the beginning of our experiment, the control animal was killed by chloroform and immediately investigated. At the same time, the "parallel" animal received the first doses causing diarrhea. The diarrhea was caused (in the second series, after infusions of senna leaves had proven ineffective) by solutions of magnesium sulfate of increasing concentrations. Cohnheim (1) described the violent action of magnesium sulfate on the dog's intestinal tract. We started with 50 - 100 cc (with the bigger animals) of a 5-7-10% solution, which was administered - according to the effect - several times every day through a throat tube. According to the physical conditions and behavior of the animals, individual doses /440 with increased concentrations of up to 25% were administered more, or less frequently. Because of violent vomiting, we occasionally had to change to a more frequent administration of small amounts. With dog No. II, we had to do an oesophagotomy when he immediately vomited everything; then 100 cc of a 25% solution were poured into the stomach and the oesophagus cut - after which death soon occurred.

In the performance of the experiments it was mandatory to have the animals lose weight as rapidly as possible, while at the same time their lives should not be endangered too early, or too suddenly. If possible, they should die spontaneously from the consequences of

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(1) O. Cohnheim and G. L. Dreyfuss. On the Physiology and Pathology of Stomachic Digestion (Zur Physiologie u. Pathologie der Magenverdauung). Zeitschrift f. physiol. Chemie, Vol. 58, p. 74, 1908.

water deprivation.

The response of the animals to whom magnesium sulfate had been administered was in general the following: several hours after administering the first doses, the defecations were in the form of feces, then of thin, bilious slime. The animals seemed to suffer from abdominal pain and howled a great deal, but were otherwise agile and only a little changed in their appearances. In all cases, small amounts of liquid were vomited. During the second day, the defecations were watery and splashy, yet always looked somewhat like feces, and smelled that way. During the following days, the animals became weaker and frailer and lay about more and more; the muscle weakness increased to an extent that the animals could only creep over the floor and on doing so, often fell to the side. The cavity of the mouth became drier, the appearance rough and run-down. Folded-up skin wrinkles began to remain in their position; finally, the skin became completely plastic and lost all tension. Water and food were occasionally offered in a tentative manner; they were almost entirely refused, or immediately vomited. 24 - 36 hours before death, complete apathy, heavy collapse and irregular breathing were observed, whereas the diarrhea stools became more seldom, and the weight reduced less rapidly. Towards the end, the respiration occurred in occasional, deep breaths.

These phenomenon coincide in general with those which other authors observed in experiments on water deprivation. It is a remarkable fact that some features exist which are also characteristic for the effects of grave nutritional disturbances in infants.

Immediately after death the animals were shaved and then very thoroughly cleaned with hot water, soap and brush. Additional work was done - as quickly as possible - in a room saturated with humidity. First the internal organs were dissected and weighed. The /441 blood flowing from the big vessels and the heart was collected separately and weighed, in addition to the squeezed-out intestinal contents.

The dissection of the control animals revealed no pathological symptoms. Similarly, the test animals showed no particular anomalies; both classes of animals had an ample panniculus adiposus; liver and spleen were evidently smaller as with the healthy animals. The mucous membranes of stomach and intestinal tract were rather reddened; the latter somewhat swollen and covered with slime.

By cuts made in the ordinary way, the head and paws (which would disturb further work), were separated. After that, during not more than an hour's time, all soft parts - skin, subcutaneous connective tissue, and musculature - were cleanly separated from the skeleton, and each piece immediately transferred into a closed glass container, which had previously been weighed. This material was then weighed, sent several times through a meat grinder, covered with alcohol and kept for approximately 8 days.

Further treatment was done in the following fashion; portions of the pulp were cooked for hours, with the repeated addition of alcohol (96%), pouring together the extracts; distillation of the alcohol and drying in the water bath. Absorption of the extracts in ether, transfer into a flask of a large Soxhlet extraction apparatus. Unification of the alcohol residue - which was not soluble in ether - with the dried material; extraction of the material, now dry like grain, and already grindable, for 24 hours. Evaporation of the ether, drying in a vacuum at 80 - 90°. In this manner, the values for fat were obtained.

The fat-free residue was once more dried on the water bath and finely pulverized in a powder mill, transferred into a glass container with a polished cover and weighted. All the samples required, together with some samples to be held in reserve, were taken on the same day from the air-dried material, and weighed. They were kept airtight under a glass bell jar in weighing containers. The samples served in determining the following values:

Total N: (Initial material 0.7 g). Determination according to the Kjeldahl method.

Dry substance: (Initial material 3.0 g). Drying in heated vacuum until the weight remains constant.

Ashes: (From the dry substance). Slow carbonization in a platinum crucible on a burner; incineration of the completely ignited substance in a muffle furnace at dark red heat. In this, the substance usually forms carbon-free ashes in such a manner that aqueous solu- /442
tions were not needed for the determinations to be performed later. The incineration in a muffle furnace can be recommended for these purposes, since one obtains fine ashes within a short time and at

relatively moderate temperatures. We checked that NaCl is not lost at the temperature used.

Cl: (Initial material 3.0g). Neumann-Volhard titration.

P : (Initial material 3.0g). Neumann decomposition; weighed as $Mg_2 P_2 O_7$ (Details according to P. Jannasch procedure).

Ca: (Residues of the chlorine determination as initial material). Precipitated in acetic acid solution as acid calcium oxylate and weighed as CaO.

Mg: (Initial material: filtrate of the Ca-determination). Weighed as $Mg_2 P_2 O_7$.

Alkali: (Initial material 5.0 g). Determined with the platinum chloride method (following, in essence, the data by Jannasch).

Si: (Initial material 20.0 g). According to Schulz [1].

S : (Initial material 1.0 g). Extracted using Carius method, filtered and weighed as $BaSO_4$ in a Neubauer crucible.

Greatest care was taken in all the analyses of ashes. Only those values of the double determinations were accepted, which coincided well; the average values were used for the computations.

In the Tables, the coarser weight determinations are rounded off to the first decimal; the values of the analysis referring to mineral substances are listed to four decimals as they were obtained. The percentage calculations were cut off at the second decimal. Even so, all values are listed with a higher accuracy than the sources of error in the entire experiment permit. Therefore, in the discussion

(1) Archiv. f. die gesamte Physiologie, Vol. 84, p. 67, 1901.

of the results, small differences are not treated, and conclusions should be drawn only from large variations.

In general, the purpose of the experiment was realized. In the first experimental series, we succeeded in maintaining animal II alive for 7 days during which sharp losses in weight occurred. This animal lost a total of 445 g; i.e., 27% of its initial weight - which amounted to 1650 g (empty intestines). The absolute daily loss amounted to 63.3 g. In the parallel experiment, animal IV was alive for 5 days and 4 hours, and lost 276 g; i.e., 29.7% of its initial weight of 927 g. The absolute values of the daily losses are smaller; those referred to per kilogram are much larger than in the first series.

It might not be unessential for the understanding of the experimental results to observe that the weight losses in the first series were rapid at the beginning, whereas the weight decreased only little /443 during the long agony of the animal. However, in the second experiment, the initial weight losses were below the daily average, and the rapid decline - starting at the end of the fourth day - resulted in the death of the animal after a shorter agony. Apart from the lesser age and the lower weight of the animal, the severity of the experimental damage is responsible for the shorter life span. Also, Czerny (1) found that his animals died sooner, the more severe were the weight losses. The fact that younger animals die more rapidly from hunger, and suffer greater losses, is in agreement with general findings.

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(1) Ad. Czerny. Experiments on the Thickening of the Blood and its Consequences (Versuche über Bluteindickung und ihr Folgen). Arch. f. exper. Patholog. u. Pharmakologie, Vol. 34, p. 268, 1894.

TABLE I

WEIGHTS AND WEIGHT LOSSES

| Dogs | I | II | III | IV | V |
|---|---|---|---|---|---|
| | 1st Experimental Series | | 2nd Experimental Series | | |
| Initial weight of the live dog | 1702.0 | 1675.0 | 851.0 | 939.0 | 950.0 |
| intestinal contents and urine | 24.1 | (24.1) | 11.4 | (11.4) | (11.4) |
| weight of live dog (intestinal contents + urine) | 1677.9 | 1650.9 | 839.5 | 927.5 | 938.5 |
| weight of dead dog (intestinal contents + urine) | 1677.9 | 1205.4 | 839.5 | 651.5 | 728.8 |
| weight loss (absolute) | ± 0 | 445.5 | ± 0 | 276.0 | 209.7 |
| weight loss per kilogram of body weight | ± 0 | 269.8 | ± 0 | 297.6 | 223.5 |
| weight loss per day (absolute) | ± 0 | 63.6 | ± 0 | 55.2 | 59.9 |
| weight loss per day and kg | ± 0 | 38.5 | ± 0 | 59.5 | 63.8 |
| duration of experiment (days) | 0 | 7 | 0 | 5 | $3^1/_2$ |

Of particular interest is the fact that the life of the test animals is endangered at approximately the same weight losses which Quest (2) calculated for human infants. The maximum weight loss which, according to him, is still compatible with the preservation of life, /444 amounts to 34% of the body weight. However, this value was only reached if the reduction was relatively slow. With a steep decline in weight within 13 days, the maximum value was 29.9% of the body weight.

(2) R. Quest. On Extreme Decreases in Body Weight of Children during the first two Years of Life (Über extreme Körpergewichtsabnahmen bei Kindern der ersten zwei Lebensjahr). Montasschrift f. Kinderheilkunde, Vol. 3, p. 453, 1905.

TABLE IIa

WEIGHT OF THE ORGANS

1st Experimental Series

| Organs | Initial Weight Dog I | Final Weight Dog II | Difference I - II |
|---|---|---|---|
| Skin + musculature | 771.0 | 481.0 | - 290.0 |
| Intestines, bladder mesentery, etc. | 140.5 | 92.0 | - 48.5 |
| Liver | 106.9 | 69.6 | - 37.3 |
| Skeleton minus (head and paws) | 196.0 | 165.7 | - 30.3 |
| Blood | 45.1 | 22.6 | - 22.5 |
| Head + paws | 238.0 | 221.5 | - 16.5 |
| Spleen | 15.4 | 3.7 | - 11.7 |
| Breast organs and tongue | 54.1 | 42.5 | - 11.6 |
| Brain + spinal cord | 43.0 | 48.9 | + 5.9 |
| Kidneys | 17.3 | 12.1 | - 5.2 |
| Total | 1627.3 | 1159.6 | 467.7 |

Although the answer has to be based on the material outlined below, the question of the reason for the death of our test animals may be raised here. It is obvious from our experiments that water losses are not solely responsible for their death. Instead - they are combined with total, or almost total food deprivation. This was neither unintentional, nor undesirable, because in the clinical conditions which inspired these investigations, water losses combine with food deprivation, in part due to clinical, and in part due to therapeutic reasons. It can be inferred from the lifespan of the animals as well as from the amount of daily weight loss that not only food deprivation is effective. For instance, a 14-day old dog /445 in Falk's experiment died on the 14th day of food deprivation, and showed a daily reduction of 4.8%. Older animals lived much longer. The highest weight reduction percentate was determined by Falk to be 8.6% in a dog just a few days old.

The contribution of the individual organs to the weight losses can be taken from Tables IIa and IIb.

TABLE IIb

WEIGHTS OF THE ORGANS (REFERRED TO 1000 g BODY WEIGHT)

2nd Experimental Series

| Organs | Initial Weight Dog III | Final Weight Dog IV | Difference III - IV | Final Weight Dog V | Difference III - V |
|---|---|---|---|---|---|
| Skin + musculature | 462.1 | 282.74 | – 179.36 | 226.8 | – 135.3 |
| Head + paws | 161.94 | 129.5 | – 32.44 | 135.0 | – 26.94 |
| Blood | 26.92 | 2.26 | – 24.66 | 3.62 | – 23.3 |
| Skeleton - (head + paws) | 125.8 | 115.9 | – 9.9 | 125.25 | – 0.55 |
| Liver | 53.01 | 43.5 | – 9.51 | 42.03 | – 10.98 |
| Intestines, bladder, mesentery, etc. | 61.35 | 55.42 | – 5.93 | 59.83 | – 1.52 |
| Breast organs + tongue | 30.49 | 24.69 | – 5.8 | 31.75 | + 1.26 |
| Spleen | 8.04 | 3.13 | – 4.91 | 5.43 | – 2.61 |
| Brain + spinal cord | 27.46 | 28.62 | + 1.16 | 29.41 | + 1.95 |
| Kidneys | 14.0 | 13.21 | – 0.79 | 12.95 | – 1.05 |
| Total | 971.11 | 698.97 | 272.14 | 772.07 | 199.04 |

These tables cannot be compared with the dogs in the first experimental series - which have the same weights. In the first experiment the original weights were noted, whereas in the second experiment the calculations were referred to an identical initial weight of 1000 g. In both experiments, all organs decreased in weight. The only exception was the central nervous system: it not only remained unchanged, but even revealed small increases. The small values which were observed may be within the limits of experimental error. However, Scheffer /446 made the same observation about his dogs which were deprived of water. In C. Voits' cats [1], brain and spinal cord did not contribute to the weight losses. With Schuchardt's pigeons, the losses amounted to negligibly small values. Thus, even in the case of extreme water losses, the central nervous system closely conserves its water. In both series, the greatest losses occur in the soft parts, head and paws, blood, and liver.

The relative losses in individual organs lead to a somewhat different order.

The spleen suffers the largest percentage loss, being reduced in the case of dog II, to a quarter of its original mass. The steep and rapid reduction of this organ has also been established several times in experiments on pure food deprivation. In the experiments of Voits the reduction in this organ amounted to 67%, and in those of Chossat [2]

(1) Hermann's Handbook of Physiology (Hermanns Handbuch der Physiologie). Vol. 6, I, p. 97, 1881.

(2) Quoted according to Voit

TABLE III

WEIGHT LOSS PER 100 g OF ORGAN

| Organ | Dog II | Dog IV | Dog V |
|---|---|---|---|
| | 1st Experimental Series | | 2nd Experimental Series |
| Spleen | 75.9 | 61.07 | 32.46 |
| Blood | 50.0 | 91.6 | 86.55 |
| Skin + muscles | 37.6 | 38.81 | 29.28 |
| Liver | 34.8 | 17.94 | 20.71 |
| Intestines, bladder, etc. | 34.5 | 9.66 | 2.49 |
| Kidneys | 30.1 | 5.64 | 7.50 |
| Breast organs | 21.5 | 19.02 | + 4.13 |
| Skeleton | 15.97 | 7.87 | 4.37 |
| Head + paws | 7.39 | 20.03 | 16.64 |
| Brain | + 13.72 | + 4.22 | + 7.01 |

to 71%. The relative reduction of the blood occurs in second place. However, no further conclusions should be drawn from these numbers. The method of extracting the blood from the heart and vessels is rather inaccurate, and strongly dependent upon the degree of coagulation. /447 For this reason alone, the values obtained from dog IV - which was processes only a few hours after his death - were too small. The smallest weight losses were found in the skeleton and in the residues of head and paws, which consist mainly of bone. The weight losses of the skin and muscles follow in third place in both experiments: they

TABLE IV

A WEIGHT LOSS OF 100 g COMPRISE THE FOLLOWING (in g):

| Organ | 1st Experimental Series | | 2nd Experimental Series |
|---|---|---|---|
| | Dog II | Dog IV | Dog V |
| Skin + muscles | 62.01 | 65.91 | 67.98 |
| Intestines, bladder, etc. | 10.37 | 2.18 | 0.76 |
| Liver | 7.97 | 3.50 | 5.55 |
| Skeleton | 6.48 | 3.64 | 0.27 |
| Blood | 4.81 | 9.06 | 11.71 |
| Head + paws | 3.52 | 11.92 | 13.51 |
| Spleen | 2.50 | 1.80 | 1.31 |
| Breast organs | 2.48 | 2.13 | - 0.63 |
| Kidneys | 1.11 | 0.29 | 0.52 |
| Brain | - 1.25 | - 0.43 | - 0.98 |
| Total | 100.00 | 100.00 | 100.00 |

are 37.6 and 38.8% respectively. In simple experiments on food and water deprivation these losses are usually exceeded by those of the liver.

If the question of how the individual organs contribute to the total weight loss is considered, or what the components of an animal weight loss of 100 g are, the soft parts assume the first place.

The soft parts with 62 and 66% contribute approximately six times the amount of any other organ in this case. Closest to these values are: dog IV, the intestines with mesentery and the connective tissue of the pelvis - 10%; with the little dog, the head and paws - 12% - i.e., the parts which contain mainly skin and muscles in addition to bones. The rest of the organs rank in rather parallel order; the glandular organs contribute little in general to the weight losses.

Our working method is thus fully justified by these results. /448 The reason being that if the assumption is correct that a large, acute weight loss means a water loss in the first place, but - on the other hand, if the soft parts contribute 60 - 70% to this loss - then the latter must be the object of further investigation, and should deal with the chemical composition of the material. The results are contained in the following Tables.

TABLE V

1 KILOGRAM OF DOG IS COMPOSED OF:
(calculated on live weight, bowels empty)

| | 1st Experimental Series | | | 2nd Experimental Series | | | | |
|---|---|---|---|---|---|---|---|---|
| | Dog I | Dog II | Diff. I—III | Dog -III | Dog IV | Diff. III—IV | Dog V | Diff IV—V |
| Skin + musculature | 459.5 | 291.4 | —168.1 | 462.1 | 282.74 | —179.36 | 326.8 | —135.3 |
| these are of: | | | | | | | | |
| Water | 244.5 | 128.0 | —116.5 | 269.7 | 153.5 | —116.2 | 186.4 | — 83.3 |
| Fat | 162.6 | 117.9 | — 44.7 | 139.2 | 85.5 | — 53.7 | 96.27 | —42.93 |
| Dry substance | 52.44 | 45.51 | — 6.93 | 53.17 | 43.74 | — 7.43 | 44.1 | — 9.07 |
| N | 7.83 | 7.0 | — 0.83 | 7.39 | 5.47 | — 1.92 | 6.36 | — 1.03 |
| Ashes | 2.69 | 1.77 | — 0.92 | 2.41 | 1.74 | — 0.67 | 2.02 | — 0.39 |

Firstly, it follows from Table V that the various test animals of both experimental series behave rather similarly: 100 g of a control dog in the first series lead to 459, and in the second series to 462 g of material to be investigated. The amounts for soft parts in the diarrhea animals are almost as close, being 290 and 283 g. The differences in the parallel animals in the first series amount to 168 and in the second to 179 g. Similarly, parallel results are obtained with respect to the chemical composition of the material; see Table VI.

In our experiments, each of the two animals of the first and second series are to be considered as one and the same individual - both before, and after the experimental weight loss. The losses of the hypothetical experimental animal result from the difference in the composition of the two parallel animals. The percentage decline of the components is presented in Table VII.

TABLE VI /449

THE FOLLOWING ARE CONTAINED IN 100 g SKIN AND MUSCULATURE:

| | 1st Experimental Series | | 2nd Experimental Series | | |
|---|---|---|---|---|---|
| | Dog I | Dog II | Dog III | Dog IV | Dog V |
| Water | 53.21 | 43.93 | 58.36 | 54.30 | 57.04 |
| Fat | 35.39 | 40.46 | 30.12 | 30.24 | 29.46 |
| Dry substance | 11.41 | 15.62 | 11.51 | 15.47 | 13.50 |
| N | 1.704 | 2.403 | 1.599 | 1.935 | 1.946 |
| Ashes | 0.584 | 0.6074 | 0.5215 | 0.6155 | 0.618 |

From Table VI it follows that the reduction of the individual components is not uniform. The water loss is by far the largest,

TABLE VII

PERCENTAGE REDUCTION OF THE INDIVIDUAL COMPONENTS

| | 1. | 2. | |
|---|---|---|---|
| | Dog II | Dog IV | Dog V |
| Water | 47.65 | 43.09 | 30.89 |
| Fat | 27.49 | 38.56 | 30.83 |
| Dry substance | 13.22 | 17.73 | 17.06 |
| N | 10.61 | 25.97 | 13.93 |
| Ashes | 34.22 | 27.83 | 16.20 |

amounting in the first series to 47.6 and in the second to 43.1%. Thus, it is not only larger than the percentage weight loss of the entire animal, but also considerably larger than the total of the weight losses of skin and muscles (37.6 and 38.8% respectively). Thus, while the amount of water has reduced to almost half of its original value, the dry substance decreased by only about 1/8 (first series, or by 1/16 (second series).

The reduction in fat obviously follows its proper laws. In the smaller animal IV, with lower fat content it is absolutely (Table V), and percentagewise (Table VI), considerably larger than with dog II. The differences become still larger if the daily fat decline per kilogram is calculated. In the first series it amounts to approximately 7 g, and in the second to approximately 10 g. General experience on the metabolism /450
during food deprivation shows that smaller animals lose relatively more fat. The question of whether the above difference can be explained in this way must remain unanswered. Apparently the fact that the liver had decreased by 35% in the larger animal, but by only 18% in the smaller animal, so that eventually larger amounts of stored glycogen limited the

fat consumption in the first animal - had to be taken into account.

Among the components of the dry substance, nitrogen shows a rather varying behavior, since with dog IV, the losses are almost doubled. Though this fact might serve to explain the greater losses of dry substance in this animal, nevertheless this fact by itself remains in part unexplained; the difference is too large to lend itself to an immediate explanation based on the weight difference between the animal due the relatively sparse material available. Straub (1) indicates that large water losses increase the protein decay. Maybe the relatively more acute, and severe water losses in the young animal had an effect to this end. Apart from fat, the losses in ashes follow the water losses, with 34.3 and 27.8% respectively, but essentially fall behind them (considering the total ashes).

The chemistry of weight reduction has its clearest expression in the listings of Table VIII, which indicate how much water, fat, dry substance, N, and ashes the organism loses upon loss of 100 g of soft parts.

TABLE VIII

A LOSS OF 100 g IN SKIN AND MUSCULATURE CONTRIBUTES (IN GRAMS):

| | 1st Series | | 2nd Series |
|---|---|---|---|
| | Dog II | Dog IV | Dog V |
| Water | 69.3 | 64.79 | 61.57 |
| Fat | 26.59 | 29.95 | 31.73 |
| Dry substance | 4.12 | 5.26 | 6.70 |
| N | 0.494 | 1.07 | 0.761 |
| Ashes | 0.547 | 0.374 | 0.288 |

(1) Loc. cit.

Here the results of the experiments approach each other more closely than in the preceding Tables and thus make it possible to realize more clearly the situation. 65 - 70% of the weight losses must be attributed to water; 25 - 30% to fat, and the dry substance contributes 4 - 5%. /451

If one compares the composition of the weight loss with that of the organ which contributed to the weight loss, one arrives at the conclusion that the composition of each are rather different. When the weight loss involved a water content of 65 - 69%, the organ which contributed to the weight loss showed a water loss of 43 - 54%, while the dry substance of the material lost amounted to 4 - 5%. The remaining material contains 15 - 16% dry substance. The decrease in the components does not proceed according to their concentration, and thus implies a shifting of the chemical equilibrium within the organs.

In view of these facts, we must again discuss the way in which our test animals fell sick and died. The appearance of the animals during their dissection indicated clearly enough that a state of extreme exhaustion did not exist. The above mentioned analysis confirmed this in a quantitative way. The smaller animal still had more than 85 g fat, and the larger more than 118 g fat in the skin and musculature. This is a contradiction to the findings in starved animals, in which the layer of fat is usually consumed, with just some traces of it left. According to C. Voit, the composition of the organs changes very little during food deprivation, even if no water

is taken, the water content hardly diminishes. It may even occur that the body begins to contain mor water during food deprivation when no water is taken (see Nothwang's pigeons). On the contrary, with forced water deprivation (e.g., by enforced feeding on dry food), one can find an increase in the dry substance of the animals, and especially in the musculature, yet such high water losses, and such an extent of concentration of body substance were never obtained in experimental studies of this problem. Therefore one can state that in the experimental series presented, the death of the animals may be attributed mainly to water losses or at least, the extreme water loss is the dominating factor in all the pathological phenomena. Conversely, the water loss can explain the behavior of the ash component. While the absolute decrease in dry substance and of fat can be regarded as a consequence of the food deprivation, it holds only with /452
certain reservations for the changes in the mineral composition which we have now to consider.

Little material is available on the behavior of organ ashes in experiments on food and water deprivation. Nothwang discovered that the ratio between dry substance and mineral substance remains unchanged in the tissue of pigeons exposed to water deprivation. However, it is changed in the tissue of starved animals. In the latter, 100 g of muscle substance free of fat contained approximately 5 g of ashes as compared with 6 g in normal animals exposed to water deprivation. Nothwang does not provide an explanation for these findings.

Since they only refer to the muscles (of pigeons), they are not particularly comparable to other results on the loss of mineral substances due to food deprivation, nor are they comparable to our material. It is generally assumed that the mineral composition percentage of the organs is only subject to small changes during food deprivation. Noorden [1] states that salts are excreted during food deprivation only to the extent to which they are set free by the consumption of tissue components, and by the decay of protein (in which they are incorporated). Experiments on metabolism show that an organism, upon being deprived of food, usually reduces its mineral consumption to a minimum. According to recent investigations by Cathcart and Fawsit [2] performed on humans deprived of food, the excretion of chlorine in urine reduces to half its original value during the first day of food deprivation. Afterwards, it falls rapidly to 1/6, and finally to very small values. The excretions of common salt during the first days are greater with carnivorous animals when fed with food rich in NaCl; nevertheless, they are small. Also the excretion of alkali declines compared with that of normal animals, so the excretion of Na goes down to 1/20 or less. The relative amount of potassium excreted is larger than that of Na because tissue containing mainly K (muscles) decreases during food deprivation (K. Katsuyama [3]). This fact must be taken into account with the relatively large K losses in our experiments.

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(1) Handbook on Pathological Metabolism (Handbuch der Pathologie des Stoffwechsels). Vol. 1, p. 521, 1906.

(2) Metabolism During Starvation. Journal of Physiology, Vol. 36, p. 27, 1907.

(3) See page 35 for this footnote.

The excretion of Ca, P, Mg and S remains relatively large. The relatively large values on the first day of food deprivation have to be discarded since our experiment begins on the second day of food deprivation. Investigations on the losses of individual tissues and organs were not made.

With only food deprivation, we would have to expect slight /453 losses of the animals' ashes due to the short duration of the experiment. If these losses were only due to a reduction of tissue substance, the change in nitrogen, or of dry substance should indicate the upper limit. This is true for the changes in the internal organs (investigated only with dog IV), in which the percentage water loss does not exceed the total percentage loss.

TABLE IX

IN 100g INITIAL DOG MATERIAL, THE INTERNAL ORGANS COMPRISE:

| | Dog III | Dog IV | Diff. III—IV | Decr. in % |
|---|---|---|---|---|
| Organs (fresh) | 221.9 | 170.8 | 51.1 | 23.03 |
| These are of: | | | | |
| Water | 178.9 | 136.0 | 42.9 | 23.98 |
| Fat | 13.16 | 8.73 | 4.43 | 33.66 |
| Dry substance | 29.81 | 26.11 | 3.70 | 12.41 |
| Ashes | 2.086 | 1.88 | 0.206 | 9.88 |

The dry substance is reduced by 12% and the ashes by 9.88%.

(3) K. Katsuyama. On the Excretion of Bases in the Urine of Rabbits under Total Food Abstinence (Über die Ausscheidung der Basen im Harn des auf absoluter Karenz gesetzten Kaninchens). Zeitschrift f. phys. Chemie, Vol. 26, p. 543, 1899.

With dog II, which we consider first, the decrease of the ash of the soft parts is more than twice as great as that of the dry substance. The comparison between the behavior of the organs and that of the soft parts is interesting also because of another reason. The water loss amounts to 23% in the first and to 43% in the latter; however, the decline in fat is approximately the same. The differences between the material lost and the remaining material are on the whole much smaller.

TABLE X

| | 100 grams of resid. org. consist of: | 100 grams of weight loss consist of: |
|---|---|---|
| Water | 79.02 (80.6) [1] | 83.95 |
| Fat | 5.11 (5.9) | 8.67 |
| Dry subst. | 15.29 (13.4) | 7.24 |
| Ashes | 1.101 (0.94) | 0.403 |

[1] Indicated in parentheses are the values for 100 grams of initial organs.

Here the conditions which hunger causes predominate - namely, a rather /454 proportional decrease of the components. This is especially true for water; the material lost is only richer in water by a few percent than the residue, whereas in the soft parts the material lost contains 65% water and the residue only 54%.

It is especially instructive to consider the individual ash components separately.

Table XII shows that the percentage decrease is not homogeneous, /455 but that differences of more than 50% exist for the individual components. S and P may have the closest correlation with N.

No judgement can be made on the behavior of tissue sulfur. As can be inferred from the table, the sulfur content of the diarrhea animal II

TABLE XI

COMPONENTS OF THE ASHES AND THEIR LOSS

1st Series 2nd Series

| | Dog I | Dog II | Diff. I-II | Dog III | Dog IV | Diff. III-IV | Dog V | Dog III-V |
|---|---|---|---|---|---|---|---|---|
| Cl | 0.4904 | 0.2253 | **0.2651** | 0.2598 | 0.1403 | **0.1195** | 0.1404 | **0.1194** |
| Na | 0.8720 | 0.3750 | **0.4970** | 0.3386 | 0.2910 | **0.0476** | 0.2946 | **0.0440** |
| K | 1.0950 | 0.5785 | **0.5165** | 0.6544 | 0.3846 | **0.2698** | 0.4144 | **0.2400** |
| Si | 0.0046 | 0.0022 | **0.0024** | — | — | — | — | — |
| P | 0.6329 | 0.4865 | **0.1464** | 0.3310 | 0.2834 | **0.0476** | 0.3227 | **0.0083** |
| Ca | 0.0854 | 0.0650 | **0.0204** | 0.0578 | 0.0225 | **0.0353** | 0.0334 | **0.0244** |
| S | 0.2576 | 0.2767 | **+0.1091** | 0.3455 | 0.3335 | **0.120** | 0.2979 | **0.0476** |

is 0.2 grams greater than that of the healthy animal. It can be assumed that this fact must be attributed to an increased resorption of some quantities of $MgSO_4$. In dog V, where this source of error is absent (see below), the sulfur loss is completely parallel to the N-loss. (Unfortunately, we do not have values for magnesium for comparison. In the initial material of 3.0 g, selected for the determination of Mg, only quantities were found which did not permit a quantitative determination. In any event, only small quantities of $MgSO_4$ can have been incorporated by resorption.)

The P-loss exceeds that of nitrogen considerably. The Ca-decrease remains on the same level. These components are to be compared with the group of substances which are easily soluble in water: Cl, Si, Na and K. Their losses are approximately 50% on the average, and come

TABLE XII

PERCENTAGE DECREASE OF THE MINERALS

| | 1st Series | 2nd Series | |
|---|---|---|---|
| | Dog II | Dog IV | Dog V |
| Cl | 54.0 | 46.0 | 45.96 |
| Na | 58.9 | 14.06 | 12.99 |
| K | 47.2 | 41.23 | 36.67 |
| Si | 52.2 | — | — |
| Ca | 23.9 | 61.07 | 42.21 |
| P | 23.1 | 14.38 | 2.51 |
| S | + | 3.47 | 13.78 |

closest to the decrease of water (47.65%). Water and salts soluble in water thus follow a similar pattern.

The situation is somewhat different with the diarrhea animal of the second experimental series. Because of the much greater N-loss, the total ashes and N-losses approach each other rather closely. However, individual components of the ashes exceed by far the N-loss. As in the first series, the decreases in Cl and K follow the water values most closely; the first with 46% is somewhat above, the latter with 41% is somewhat below the water loss of 43%. But the values for sodium and calcium differ sharply, since the lost quantities of the first are much smaller, and those of the latter much greater. In this case, the loss of P is smaller also. The S-content has not increased, but decreased only to a small extent. With respect to Mg, the statements concerning dog II are also valid.

Since these losses of mineral substances are greater than the losses corresponding to food deprivation, the only possible interpretation is that they are closely related to water. The assumption that a large water loss leads to an increased concentration of the tissue components would be only partially correct in this case. Certainly a shift in the ratio of the components occurs due to the rapid decrease of water; the consumption of fat and dry substance cannot be compared with that of the components. However, the same may hold only for some ash components. Analogous quantities of the rest of them are excreted simultaneously with the water or soon afterwards. /456

Various types of relations between water and salts appear possible. It cannot be excluded off-hand that the strong intestinal irritation, which was imposed, provoked a marked functioning of bowels and gland secretions containing minerals, or that the mechanism of excretion through the intestines and kidneys implied the co-transport of salts. It was, therefore, necessary to investigate whether the release of great amounts of chemically pure water also could cause a corresponding excretion of minerals.

The experiment with dog V, the third animal of the second experimental series, was devoted to this problem. The results of this experiment are listed in all the tables in a side column. The corresponding animal for comparison is dog III. The water was extracted from dog V not through the intestines; the animal was transferred into a place with a hot atmosphere of dry air to make him lose water by perspiration. Because of external reasons, it was not possible to maintain the temperature of this place quite constant and to keep it on the desired level.

The observation, which Czerny made with his cats, could be confirmed: up to a certain temperature, the general condition of the animal is relatively little affected; above that temperature, the increase by each additional degree has a deleterious effect; the rate of water excretion has an influence upon the life span. At 37° the animal became very short of breath and very disturbed so that it could be kept at this temperature only four hours, whereafter it was permitted to recover outside the case. In the first two days the animal weight decreased by 100 g, and very little the following day. After that, when he was left overnight at approximately 38°, he was found dead the next morning. His life span was approximately 3 1/2 days, the weight loss (Table I) amounted to 209.7 g or 22.3%. With 64%, the loss per kilogram and per day was the greatest observed. The losses in the individual organs are rather parallel to those of animal IV with diarrhea, but are somewhat smaller. Only the breast organs show a different behavior: they became heavier, like the brain - perhaps due to the kind of death /257 experienced by the animal. Skin and musculature contribute the largest value to the total loss, namely 68% (Table IV).

The chemical analysis shows that the fat decrease is lower in percentage, as well as in absolute value, corresponding to the shorter lifetime (Tables V and VI). The loss of dry substance is almost equal to that of the dog with diarrhea, whereas considerably less N was lost. For the latter fact we do not have an interpretation; the only possible interpretation would be according to Straub, that the decomposition products could be removed only insufficiently because of the early death. However, this cannot be proven.

The water loss amounts to 31% and is smaller than with the magnesium animal by approximately 1/3; the ashes loss is 10.2% and 2/5 smaller. Three of the ash components show losses which exceed the water loss. The greatest differences are found with Ca and P, and do not fit into any plausible interpretation. The percentage decreases of the water soluble substances differ only slightly from those of animal IV; here, they are on an average 31.8%; with dog IV they are 37.7%. Just as in the first experimental series, the percentage losses of water and of water soluble minerals are parallel. Since other factors do not affect the values of S in this case, the latter has the expected ratio to N. With their losses of 13.8 and 13.9%, these substances show a very close parallelism.

The experiment with dog V proves that the water does not carry minerals, because it might be excreted through the intestines or kidneys only in the form of a salt solution, but that the water loss per se results in the loss of certain quantities of salts.

It is not known in what fashion the processes are interrelated in the one or the other case. However, it is necessary for the further treatment of the problem to discuss the available possibilities in the form of a hypothesis. According to the present state of our knowledge, the entire process can be considered as follows. The presence of large quantities of concentrated and practically unresorbable magnesium sulfate solution may draw a large amount of water into the intestines. It can stem only from the blood, so that the blood becomes thickened. The blood composition remains closely fixed at constant values; it is most /458
easily corrected by water flowing from the organism's water deposits,

if no water is taken. During a severe water loss, the blood has no time to supplement its water content; it can at best prevent a further thickening. Up to this point the situation is relatively clear; but where can one find that tissue water, in what form is it present, and in what way is it transferred to the blood? The process cannot follow the simple laws of osmosis, because then salt ions would have to migrate into the tissue, in accordance with the outgoing water; and the tissue salt concentration should be increased instead of reduced. Water of two types is in the tissue: first, the water of the muscle tissue itself. We know that it is rich in sodium and poor in potassium and phosphoric acid. Second, the water which is situated between the individual muscle fibers and muscle bundles. The investigations of Overton[1] made it appear likely that this in-between liquid is essentially a solution of common salt. Much evidence speaks in favor of the assumption that this in-between liquid containing Na serves, in the first place, to release water, and only after that the fiber itself. Clinical observations can be quoted for a further clarification. They show that in acute water losses, three degrees or stages can be distinguished. They cannot always be clearly separated in time, but, apparently, at any of these stages the process may come to a stop. If a normal individual loses a certain moderate amount of water due to some external influence (e.g., perspiration process, state of thirst), the water taken to satisfy the

(1) C. Overton. Contributions to the General Physiology of Muscles and Nerves (Beiträge zur allgemeinen Muskel- und Nervenphysiologie). Archiv für die ges. Physiologie, Vol. 92, p. 115, 1902.

immediately arising thirst can completely restore the individual ad integrum within a short time. We assume that, besides the blood, the liquid between the muscles (which corresponds in essence to a NaCl solution) loses water and then recaptures enough of the water provided until the normal concentration is restored. Variations in the water content, which do not exceed this extent, are compatible with a healthy condition. In this first case, the water loss may be called a concentration loss, because we have to assume that the concentration in the tissue liquid is increased temporarily due to a water loss. Such losses remain within /459
the limit of variability of the water content.

The restoration capability is affected if the water loss is greater, or if restitution is not possible within a short time. With infants, such cases usually can be clearly realized by a decrease of the skin turgor. In this case, with a water or milk/water diet the weight curve rises only slowly to its former level; it reaches the latter faster when small amounts of common salt are administered, without edemas resulting. The organism's marked retention of NaCl after a weight loss of this type and the rapid rise of the weight curve by the common salt indicate that, in such a case, common salt was lost along with the water(*). Thus, also in this case, there is a tendency to conserve a constant composition in the organism. Losses of this type exceed the limits of physiological variations. They may be called reduction losses, because the mineral

(*) This assumption finds interesting illustration through the observations of Cohnheim and Kreglinger which have just appeared: Contributions to the Physiology of Water and of Common Salt (Beiträge zur Physiologie des Wassers und des Kochsalzes). Zeitschrift f. Physiol. Chem., Vol. 63, p. 413, 1909.

content is reduced, together with the water, maintaining the normal concentration.

Water losses of the third kind occur only in connection with conditions of grave diseases. Among these are the weight losses of our test animals and those of infants with severe nutritional disturbances (stages of decomposition and poisoning, according to Finkelstein). Clinically, one can say that they threaten life from a certain point on, and that they are hard to remedy. Even under the most favorable conditions, the recovery time is a multiple of the time during which they originated. Addition of common salt shifts the weight curve slightly upwards, or even leads to the formation of edemas. All of this indicates that these quantities of water are no longer supplied merely by displacement processes of the interstitial liquid.

This concept finds further support from our experimental results. As has been mentioned before, the in-between liquid is rich in sodium and low in K, while the contrary is the case in tissue, especially in muscle fibers. In the losses with which we are concerned, the release of po- /460
tassium regularly exceeds (sometimes even considerably) that of sodium and chlorine. Moreover, the P:N ratio has been shifted at the expense of P. This points to the loss of non-proteinic P; losses of Si and Ca could be established. More complicated chemical bonds must have been broken up and debris flushed out. We are inclined to assume that the tissues (especially connective tissue and muscles) contain one or several unstable components which decay under certain conditions (infections, poisoning, concentration variations of the blood, fever?) and let their water flow out in large quantities. Since tissue substance is broken

up on this occasion, we call them destruction losses. In organic chemistry, compounds are known which are capable of binding large quantities of water in themselves, but relatively easily lose this binding capability. Water and salts could be bound to colloidal albuminous substances. We would like to mention that with infants such severe weight losses are always accompanied by a strong decomposition of protein.

The detailed course of the process may be as follows: the main quantity of the water, which had been set free, flows into the colloidal, surrounding solution (which is concentrated), while the corresponding solid components follow more slowly, as far as they exist in excess. This situation appears likely because of the fact that, with dog II who lived more than 24 hours after the maximum weight loss, the excretion of ash components attained the percentage level of the water loss. However, in the second experimental series, in which death occurred more rapidly, the excretion of ashes lagged behind that of water. This holds true to a greater extent with dog V; he lost his water (31%) very rapidly and died during the maximum weight loss. With the three animals, the ratio of ash loss to water loss is:

II: 1 : 126.7

IV: 1 : 173.2

V: 1 : 213.8

In our experiments, there is no serious doubt as to whether salts or water were primarily excreted. If we want to compare weight losses of sick infants with our experiments, we must also consider those cases in which water losses through the intestines play a minor role, but where primary demineralization is possible due to the action which acid decomposition products of fat and carbohydrates exert on mineral substances. In these cases, the main portion of water is probably lost by perspiration. Nothing invalidates the assumption that the processes can also occur in the converse causal sequence. /461

Overton's investigations, to which we referred here, deal only with muscles. Skin and subcutaneous tissue form an essential component in our investigation material. We do not know which part of the water loss pertains to these. According to Wahlgren[(1)], skin has an essentially higher Cl-content than the musculature; more than a third of the body's entire chlorine is contained in it. It is possible that the muscles' contribution in "concentration and reduction losses" is significant. Clinical data should be consulted for this matter.

For the time being, there is still some doubt as to whether the actual results of our experiments occur in the manner postulated in this article, or in some other way. Clinical and experimental observations can be understood in a relatively satisfactory way with the interpretation which we have offered, and new questions can be initiated. However, in no case should their value be overestimated. The results of these animal experiments cannot be transferred to humans without additional proof. Their application for the discussion of human pathology processes is possible only with great reservations. Although many factors

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(1) V. Wahlgren. "The Meaning of Tissue as a Storehouse of Chlorine" (Über die Bedeutung der Gewebe als Chlordepots). Archiv f. exp. Pathol. u. Pharmakolog, Vol. 61, p. 97, 1909.

point to similarities in principle, one can assume that large differences in details might be discovered. For instance, it is very likely that with infants the skin tissue and the subcutaneous tissue are richer in water than with dogs, and participate more in the release of water. This would be in agreement with the assumption that Cl might be of greater importance than with carnivorous animals. Yet, for both cases, it is true that alkalis participate in the water balance, and not only in the form of chlorides. Meyer(1) and Schloss(2) showed this in the case of infants; Blum(3), among others, demonstrated this in the case of adults. A simple calculation in our material shows that not all alkalis can have been lost in the form of chlorides. One can then readily understand why an equivalent restitution of destructive losses /462 cannot be achieved by providing NaCl, whereas smaller variations may be corrected by water alone. Thus, occasionally infants show a weight increase on a water diet. If rapid weight losses change the proportional composition of the body in the case of human infants also, and lead to similarly large salt losses in the tissues and secretions, as has been observed here, then the destructive action of weight losses is made more understandable. If complicated chemical compounds are destroyed during water losses, then it is understandable that true recovery can occur only under certain nutritional conditions, and even then can proceed

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(1) Proceedings of the Society for Child Medicine (Verhandlungen d. Gesellschaft f. Kinderheilkunde). Salzburg, 1909.

(2) Biochemische Zeitschrift, Vol. 22, p. 283, 1909.

(3) 26th Congress for Internal Medicine (26. Kongrel f. innere Medizin). Wiesbaden, 1909.

only slowly.


## Summary

1. Weight losses of 25-30% of the body's weight, occurring within a few days and having fatal consequences, can be caused experimentally by severe diarrhea.

2. The various organs participate in the weight losses to a varying degree. Skin and musculature ("soft parts") show the largest loss; they contribute approximately 65% of the loss.

3. The chemical components of the soft parts are not reduced uniformly. The water is most severely affected (losses up to 50%). After that, the ash components follow with relatively large losses.

In 100 g of weight loss of the soft parts, there are 65 to 75 g of water. The normal water content of the same organs amounts to only 55%.

4. The individual ash components show a very different behavior. The percentage losses of Cl and K are closest to those of water. In addition, in one case the losses of Na and Si are also close to those of water. It can be shown that an intrinsic relation exists between the losses of water and of salt.

5. The release of larger quantities of physiological body water is not only connected with losses of common salt, but also implies more complicated changes in the salt contents of the body.

6. It is likely that the excretions of water and salt are not of the same degree, but that the excretion of mineral substances follows somewhat more slowly after the water loss.

7. Similar relations between water and salts result also when large /463

water losses have been caused by perspiration.

8. The internal organs show a behavior different from that of the soft parts; they maintain their composition approximately.

9. In connection with clinical observations, it can be assumed that three essentially different degrees or stages of water loss must be distinguished (concentration losses, reduction losses, destructive losses).

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